IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Kink, John A..
Serial No.: 09/095,536 Group No.: 1646
Filed: 06/10/98 Examiner: Murphy, J.
Entitled: **Prevention and Treatment of Sepsis**

DECLARATION OF DOUGLAS C. STAFFORD UNDER 37 C.F.R. § 1.131

Assistant Commissioner for Patents
Washington, D.C. 20231

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Dated: 6-7-01 By: Mary Ellen Waite
Mary Ellen Waite

Dear Examiner:

1. I, Douglas C. Stafford, was President of Ophidian Pharmaceuticals, Inc. ("Ophidian") from August 1990 through August 2000. Furthermore, Ophidian was the assignee of this patent application when it was filed on June 10, 1998.

2. I had either direct or indirect supervisory responsibility for certain experimentation at Ophidian that has relevance to the subject matter in the above-referenced patent application. I have a Ph.D. degree in immunology and 15 years experience in commercial biologic product development and was involved in the design and interpretation of studies described below.

3. I have read and understand the above-captioned patent application and have read the Office Action from the Patent Office mailed February 7, 2001. Furthermore, I am aware of the cited reference by Marilyn A. Coleman (WO 98/14209).

4. Prior to filing the above-captioned patent application, a series of experiments were performed by Ophidian scientists to evaluate the effectiveness of antibodies to cytokines in resolving various immune/inflammatory conditions in animal disease models. In one example, a rodent sepsis model was used to evaluate the effectiveness of antibodies to tumor necrosis factor (TNF) and interleukin 6 (IL-6). Briefly, animals were given galactosamine and

lipopolysaccharide, which the literature has shown to cause death in mice. Animals were then monitored to determine if injected antibodies to TNF and/or IL-6 could prevent mortality.

5. The summary of this experiment was recorded in Ophidian research notebook number 304, page 86, with the entry signed by Mr. Bruce Thalley (the results were counter-signed by Ms. Denise Hottmann, indicating that the results were "read and understood"). Here, results showed that antibodies to TNF and IL-6 were effective in preventing mortality. In summarizing this experiment, Mr. Thalley wrote "[c]ombination therapy appears to protect mice at least 2 h after LPS challenge."

6. This research record shows that the invention set forth in the above-captioned patent application was conceived and reduced to practice prior to publication of the Coleman reference cited by the Patent Office.

The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under §1001 of Title 18 of the United States Code, and that such willful false statements many jeopardize the validity of the application or any patent issuing therefrom.

Date: June 8, 2001 Signed: _____
Douglas C. Stafford, Ph.D.